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Uterine Leiomyosarcoma Manifesting as a Tricuspid Valve Mass

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Key Words

Leiomyosarcoma · Tricuspid valve · Metastasis · Pulmonary embolism

Abstract

Uterine leiomyosarcoma is a rare malignancy and carries a poorer prognosis when compared to endometrial carcinoma. It has been observed to metastasize to all the major organs. It presents with symptoms of abdominal distension, vaginal bleeding and may pass unnoticed until an advanced stage in patients with leiomyomas. Surgery is a viable option in patients with disease limited to the uterus, but metastasis to the heart may require surgery to prevent acute and catastrophic complications. The case described here involves metastasis to the tricuspid valve, which caused severe tricuspid regurgitation in the setting of acute pulmonary embolism. Surgical resection restored cardiac function and stabilized the patient. This case illustrates a rare site of metastasis of leiomyosarcoma which required immediate intervention and resulted in a favorable outcome.

Introduction

Leiomyosarcoma is a malignancy of the soft tissue and accounts for 5–10% of soft tissue sarcomas [1]. Leiomyosarcomas are histologically similar, occur in varied locations, with the retroperitoneum being the most common site, and are spread by hematogenous route [2]. Uterine leiomyosarcomas are more aggressive and carry a poor prognosis irrespective of the stage of presentation [3]. They may be present in the uterus with leiomyomas, and both

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tumors may express the estrogen receptor (ER) and the progesterone receptor (PR) [4]. The presence of 2 out of the 3 Stanford criteria, namely: prominent cellular atypia, areas of tumor necrosis and abundant mitoses has been correlated with a >10% risk of metastasis [5].

Uterine leiomyosarcomas have been known to metastasize to distant organs. They often present as vaginal bleeding and may be detected by ultrasound imaging during initial workup. The incidence of leiomyosarcoma in African-American woman is approximately 2-fold higher than in Caucasian women [6]. Tamoxifen usage and pelvic radiation may increase the risk of development of uterine sarcoma [7–9]. The presence of symptoms such as an enlarged uterus, vaginal bleeding, abdominal distension, urinary frequency, etc., in a postmenopausal woman with a prior history of leiomyomas should raise the suspicion of leiomyosarcoma.

Uterine leiomyosarcomas have been known to spread to distant sites including the lung, abdomen, brain, breast, bone, skin, pancreas and kidney [10–17]. Brain metastasis has been rarely observed and peritoneal sarcomatosis has been occasionally documented [16, 18]. It is rare to detect an ER- and PR-positive mass actively growing on a heart valve. This case highlights the unusual presentation of uterine leiomyosarcoma as a mass attached to the tricuspid valve (TV). The location of the mass may contribute to hemodynamic instability and surgical intervention may be required immediately after presentation.

Case Summary

The patient is a 49-year-old woman with a past medical history significant for uterine fibroids and menorrhagia who presented with a complaint of heavy vaginal bleeding over the previous 8 days, progressive weakness, lightheadedness, palpitations, dyspnea on exertion and lower abdominal pain. She denied chest pain, cough, hemoptysis, fever and sick contacts. Her uterine fibroids were treated in the past by blood transfusion and bilateral uterine artery and left ovarian artery embolization. She was treated for tuberculosis and was hepatitis C positive. She was not allergic to any medications and denied smoking tobacco, consuming alcohol or using intravenous drugs. She was noted to have a hemoglobin level of 5.1 g/dl and received 5 units of packed red blood cells and levonorgestrel. Her shortness of breath improved marginally but she continued to have tachycardia. She was noted to have left lower extremity swelling which the patient admitted had started 4–5 days prior to admission.

A lower extremity Doppler ultrasound revealed extensive deep venous thrombosis and she was started on systemic anticoagulation with dalteparin. Her chest X-ray revealed multiple bilateral pulmonary nodules (fig. 1a, b). A chest CT showed saddle embolus and multiple bilateral pulmonary emboli with evidence of right heart strain. Multiple bilateral pulmonary nodules suspicious for metastatic disease and a moderate right-sided pleural effusion and a trace left-sided pleural effusion were also noted (fig. 2). Her physical examination was pertinent for tachycardia, normal breath sounds, distended abdomen with tenderness to palpation in the lower quadrants (uterus was palpable) and bilateral calf muscle swelling with tenderness. She underwent placement of an inferior vena cava filter and an endometrial biopsy. However, the next day morning the patient was noted to become severely hypoxemic with an altered mental state. She was intubated and started on vasopressors for shock.

Due to persistent hypoxemia and hypotension she was taken to the operating room for thrombectomy. Intraoperative transesophageal echocardiography revealed an underfilled left ventricle with interventricular septum flattening, massively dilated right atrium and an

extremely dilated right ventricle with reduced function. It also showed a mild-to-moderate pulmonary artery (PA) dilatation with a large mass in the right PA (possibly thrombus) and a severe tricuspid regurgitation with a large pedunculated, very mobile mass attached to the TV leaflets that moved from the right atrium to the right ventricle during the cardiac cycle (fig. 3). Intraoperatively, a large thrombus at the bifurcation of the PA which was extending into the PA branches was removed. The right atrium and the right ventricle were found to be devoid of any clots, but a worm-like mass attached to the anterior TV leaflet was identified and removed. Also a left lower lobe wedge resection was performed on a peripheral nodule and the right pleural effusion was drained.

The patient continued to require a maximal dose of vasopressors and had to be maintained on extracorporeal membrane oxygenation and renal replacement therapy. She was successfully extubated on postoperative day 6 and was transferred to the medical floor. Histology of the mass attached to the TV and the pulmonary nodule revealed spindle cells with marked nuclear atypia, frequent mitoses, extensive necrosis and vascular invasion consistent with leiomyosarcoma (fig. 4a). Immunohistochemistry was positive for smooth muscle actin (SMA), desmin, ER, PR and cyclin-dependent kinase inhibitor 2A (p16) (fig. 4b–f). It was negative for myogenin, myogenic differentiation 1 (myoD1) and cytokeratins (AE1/3).

These findings support a diagnosis of leiomyosarcoma and likely represent metastasis from the uterus. The pleural fluid showed rare, isolated highly atypical cells of uncertain origin and scattered mesothelial cells. The endometrial biopsy revealed an early secretory endometrium. It is likely that this patient suffered from a massive pulmonary embolism due to a combination of a predisposed state of hypercoagulation due to malignancy and due to the possible obstructive nature of the mass on the TV. These findings suggest that uterine leiomyosarcoma may manifest itself as a mass on the heart valves, and early identification may help prevent life-threatening complications.

Discussion

Uterine leiomyosarcoma is a rare malignancy and comprises about 1% of uterine malignancies, with an annual incidence of 0.64/100,000 women [19]. The histopathological diagnosis is often made after hysterectomy as endometrial biopsies or dilatation and curettage may not yield adequate tissue [20]. These tumors are thought to arise independently and less than 5% of them arise from transformation of preexisting leiomyoma [21]. They differ from leiomyomas and smooth muscle tumors of uncertain malignant potential (STUMP) by the presence of atypia, mitoses and tumor necrosis [22]. These tumors often present in the fifth decade of life, usually as a pelvic mass with vaginal bleeding [23]. On CT and MRI imaging they may present as submucosal, intramural or subserosal masses which are heterogeneously enhancing with hemorrhage or calcifications [24, 25].

Definitively differentiating the radiological appearance of leiomyosarcomas from leiomyomas has not been successful and histopathological diagnosis continues to be the standard. The size and rapidity of growth may indicate malignancy but are not considered reliable indicators [26]. There is a low propensity for pelvic node involvement, but CT has been the most common imaging modality for investigating the presence and extent of extra-uterine disease and distant metastasis [27]. Imaging by ultrasound may reveal increased vascularity indicative of malignancy [28]. Further investigation is required for FDG-PET to be established as an imaging modality for leiomyosarcomas [29].

The stage of the disease, mitotic count and tumor grade have been shown to be significant factors to help determine the prognosis [23]. Hysterectomy has been the main stay of treatment with preservation of the ovaries, but pelvic lymphadenectomy has not been advocated due to the low involvement of pelvic lymph nodes [23, 30]. Surgical reduction has been advocated in patients with localized single foci [31]. Doxorubicin had been the agent of choice until a combination of gemcitabine and docetaxel was found to have an overall response rate of 53% in patients with advanced unresectable uterine leiomyosarcoma [32]. Trabectedin has been approved for use in Europe and is being currently investigated in combination with doxorubicin [33, 34]. Hormonal agents such as megestrol, medroxyprogesterone and aromatase inhibitors are being investigated, but the increased risk of side effects like venous thromboembolism and osteoporosis are being recognized as impediments to their use [35, 36]. Radiotherapy has been shown to help improve pelvic control, but there is no evidence for similar benefit for distant metastasis [37].

Disclosure Statement

The authors declare that there was no funding for this study.

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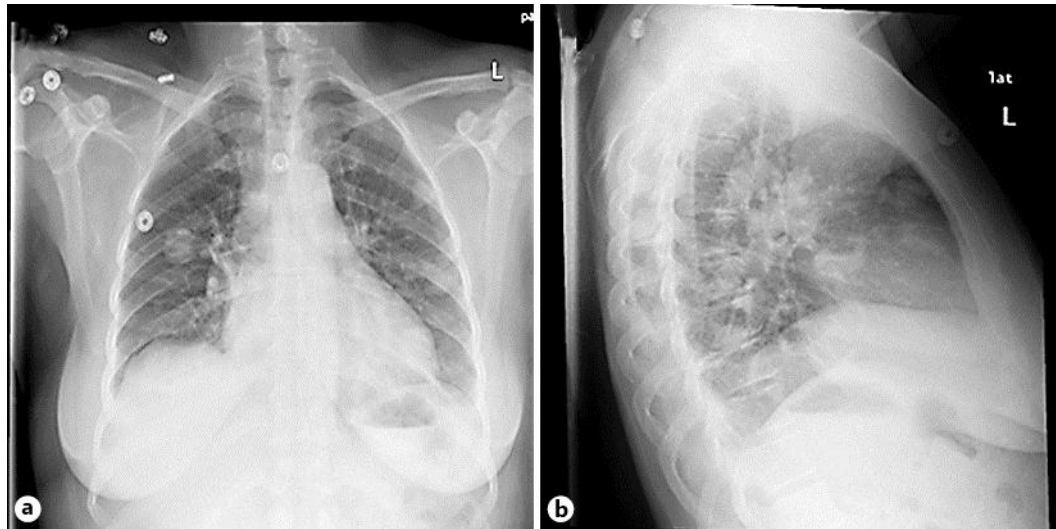


Fig. 1. **a** PA view of chest X-ray showing numerous pulmonary nodules. **b** Lateral view of chest X-ray showing pulmonary nodules.



Fig. 2. Chest CT with contrast showing pulmonary nodules and a moderate right-sided pleural effusion.

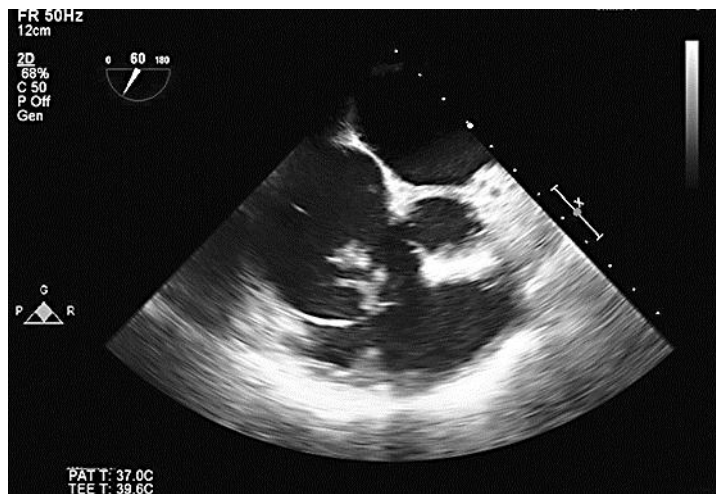


Fig. 3. Transesophageal echocardiogram showing a large pedunculated mass attached to the TV.

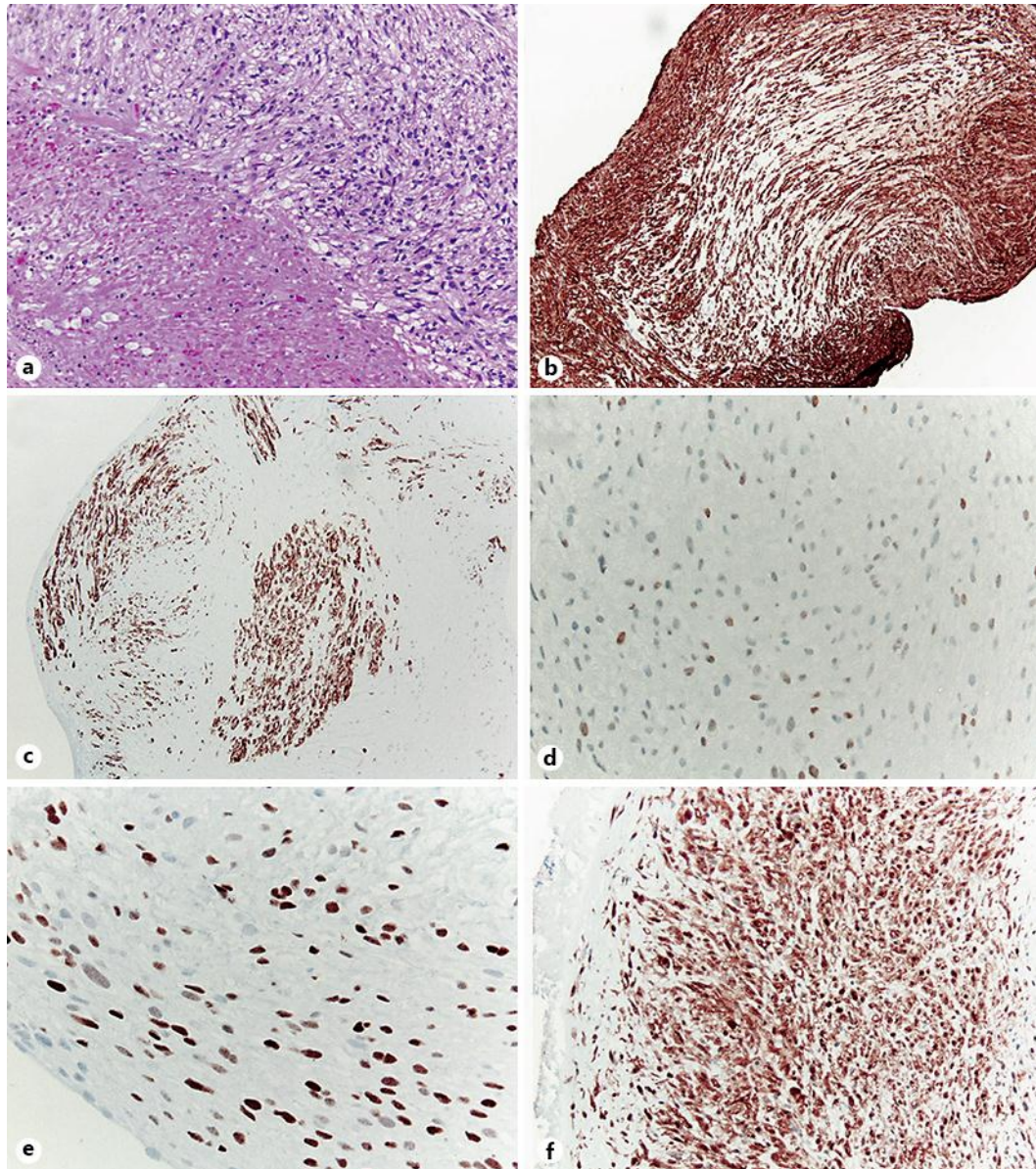


Fig. 4. **a** Hematoxylin and eosin staining showing spindle cells with nuclear atypia on the right and necrosis on the left side. **b** Immunostaining for SMA of the mass resected from the TV showing myofibroblasts. **c** Immunostaining for desmin of the mass resected from the TV showing myofibroblasts with smooth muscle differentiation. **d** Immunostaining for ER of the mass resected from the TV indicating its likely uterine origin. **e** Immunostaining for PR of the mass resected from the TV indicating its likely uterine origin. **f** Immunostaining for cyclin-dependent kinase inhibitor 2A (p16) of the mass resected from the TV which helps distinguish it from leiomyoma.